

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

SEDRANI ET AL.

APPLICATION NO:

FILED:

FOR: RAPAMYCIN ASSAY

Assistant Commissioner for Patents  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to the calculation of the filing fee, please enter the following amendment.

IN THE SPECIFICATION:

Page 1, after the Title, insert:

-- This is a divisional of Ser. No. 09/585,743, June 2, 2000, pending, which is a division of Ser. No. 09/072,278, May 4, 1998, pending, which is a continuation of Ser. No. 08/532,837, October 5, 1995, abandoned, which is a 371 of PCT/EP94/01006. March 30. 1994. --

IN THE CLAIMS:

Cancel claims 1-14 and add claims 15-~~18~~:

- 15. (new) A monoclonal antibody capable of specifically recognizing a rapamycin.
16. (new) A monoclonal antibody of claim 15 capable of recognizing an epitope on the FKBP-binding portion of a rapamycin.
17. (new) A monoclonal antibody of claim 15 capable of recognizing an epitope on the effector portion of a rapamycin.
18. (new) A monoclonal antibody of claim 15, obtained or obtainable by:

- a) reaction of a rapamycin having an activated coupling group with an immunogenic protein to produce an immunogenic conjugate,
- b) administration of said immunogenic conjugate to an appropriate animal species to effect immunogenic challenge and recovery of antibody-producing cells sensitized to said conjugate,
- c) immortalization of said antibody-producing cells, and
- d) recovery of monoclonal antibody from a selected immortalized cell line thus established.

19. (new) A monoclonal antibody of claim 15 wherein the rapamycin is (i) rapamycin; or (ii) a 40-O-alkylated rapamycin, preferably wherein the 40-O-alkyl substituent is selected from hydroxyalkyl, hydroxyalkoxyalkyl, acylaminoalkyl, or aminoalkyl.

20. (new) A monoclonal antibody of claim 19 wherein the rapamycin is selected from

- i) 40-O-(2-hydroxyethyl)-rapamycin,
- ii) 40-O-(3-hydroxypropyl)-rapamycin,
- iii) 40-O-[2-(2-hydroxy)ethoxy]ethyl-rapamycin, and
- iv) 40-O-(2-acetarninoethyl)-rapamycin).

21. (new) A monoclonal antibody of claim 15 capable of distinguishing between (i) rapamycin; and (ii) a 40-O-alkylated rapamycin, preferably wherein the 40-O-alkyl substituent is selected from hydroxyalkyl, hydroxyalkoxyalkyl, acylaminoalkyl, or aminoalkyl.

22. (new) An immunogenic conjugate comprising a rapamycin portion and a protein portion.

23. (new) An immunogenic conjugate of claim 22 which is produced by reacting a protein with a rapamycin derivative bearing an activated coupling group.

24. (new) An immunogenic conjugate of claim 23 wherein the rapamycin derivative is

- i) 40-O-succinimidooxysuccinyl-rapamycin,
- ii) 28-O-succinimidooxysuccinyl-rapamycin, or
- iii) 28-O-(succinimidooxysuccinyl)-40-O-(2-hydroxyethyl)-rapamycin.

25. (new) A rapamycin having an activated coupling group.

26. (new) A rapamycin of claim 25 selected from

- i) 40-O-succinimidooxysuccinyl-rapamycin,
- ii) 28-O-succinimidooxysuccinyl-rapamycin, or
- iii) 28-O-(succinimidooxysuccinyl)-40-O-(2-hydroxy)ethyl- rapamycin.

27. (new) A hybridoma cell line capable of producing a monoclonal antibody of claim 15.

28. (new) An immunoassay kit for measuring the blood level of a rapamycin, comprising a monoclonal antibody of claim 15. --

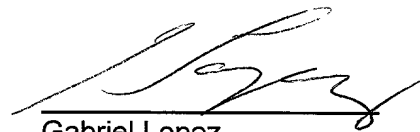
#### REMARKS

The claims have been amended to eliminate multiple dependencies.

Early and favorable consideration of the claims is respectfully awaited.

Respectfully submitted,

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